Synthesis and Physical Properties of Normal Higher Alcohols. I. Synthesis of Normal Higher Primary Alcohols of Odd Carbon Numbers from Undecanol to Pentacosanol

By Akira WATANABE*

(Received March 17, 1959)

As part of a broad program of investigating the synthesis and physical properties of long chain compounds, the present author has taken up normal primary alcohols. Since Müller[1] reported an X-ray investigation of a series of normal paraffins, a phenomenon of phase transitions in the solid state of long chain compounds has drawn much attention of chemists and physicists.

Although several communications dealing with the transition phenomenon of long chain compounds have appeared in the literature, higher alcohols have not been studied as fully as paraffins and consequently the results are rather fragmentary and somewhat ambiguous. Moreover, only few reports are found on the alcohols with odd carbon numbers and more than eighteen carbon atoms[2]. A reason for this may have been the difficulty of obtaining a series of higher alcohols in high purity. Therefore, it is desirable to investigate in more detail and more systematically the synthesis and the physical properties of the series of alcohols. From this point of view, the author has undertaken to synthesize alcohols having more than ten carbon atoms and in this paper the preparation of higher alcohols of odd carbon numbers from undecanol $C_{11}H_{23}OH$ to pentacosanol $C_{25}H_{51}OH$ is reported.

Until recently, all the alcohols up to hexatriacontanol $C_{36}H_{73}OH$ have been synthesized by other workers for the purpose of making comparison with naturally occurring products. In the present investigation, the three synthetic routes were chosen depending upon the availability of starting materials and close attention was paid to obtain the products having sufficient purity for physical studies.

(A) $RCO_2H \rightarrow RCO_2Ag \xrightarrow[\text{(in } CCl_4)]{Br_2} RBr$

$\xrightarrow{CH_3CO_2Ag} CH_3CO_2R \xrightarrow{H_2O} ROH$

(B) $RCO_2H \xrightarrow{SOCl_2} RCOCl \xrightarrow{CH_2N_2} RCOCHN_2$

$\xrightarrow[\text{(in } CH_3OH)]{Ag_2O} RCH_2CO_2CH_3 \xrightarrow{LiAlH_4} RCH_2CH_2OH$

(C) $\underset{\text{(I)}}{C_2H_5O_2C(CH_2)_5Br} \xrightarrow{\text{Ethyl malonate}}$

$\underset{\text{(II)}}{C_2H_5O_2C(CH_2)_5CH(CO_2C_2H_5)_2} \xrightarrow[Na]{C_6H_5CH_2OH}$

$\underset{\text{(III)}}{C_6H_5CH_2O_2C(CH_2)_5CNa(CO_2CH_2C_6H_5)_2} \xrightarrow{RCOCl}$

$\underset{\text{(IV)}}{C_6H_5CH_2O_2C(CH_2)_5C(CO_2CH_2C_6H_5)_2COR} \xrightarrow[2.\ -CO_2]{1.\ H_2}$

$\underset{\text{(V)}}{RCO(CH_2)_6CO_2H} \xrightarrow{\text{Huang-Minlon reduction}}$

$\underset{\text{(VI)}}{R(CH_2)_7CO_2H} \rightarrow \underset{\text{(VII)}}{R(CH_2)_7CO_2C_2H_5}$

$\xrightarrow{LiAlH_4} \underset{\text{(VIII)}}{R(CH_2)_8OH}$

Undecanol $C_{11}H_{23}OH$, tridecanol $C_{13}H_{27}OH$, pentadecanol $C_{15}H_{31}OH$, heptadecanol $C_{17}H_{35}OH$ and heneicosanol $C_{21}H_{43}OH$ were prepared by method A. The process of degradative bromination of silver salts of fatty acids is the well known Hunsdiecker reaction[3]. The alkyl bromides obtained by this method were heated with silver acetate at 150°C without a solvent to yield the acetyl compounds which were converted into the desired alcohols by hydrolysis with alcoholic potassium hydroxide. Overall yields were about 40%.

Nonadecanol $C_{19}H_{39}OH$ was prepared by the Arndt-Eistert reaction (method B) from stearic acid. Stearoyl chloride, obtained from stearic acid and thionyl chloride, and diazomethane in ether gave

---

* Some parts of this work were perfomed of Department of Chemisty, Faculty of Science, Kyoto University Sakyo-ku, Kyoto.

[1] A. Müller, *Proc. Roy. Soc.*, **A138**, 514 (1932).

[2] Review of the literature is presented in a paper by Kakiuchi et al., *J. Phys. Soc. Japan*, **75**, 291 (1950).

[3] H. Hunsdiecker and Cl. Hunsdiecker, *Ber.*, **75**, 291 (1942).

TABLE I. ALCOHOLS

Alcohols	Formula	Analyses, % Calcd. C	Calcd. H	Found C	Found H	m. p.*, °C		t. p.**, °C
Undecyl	$C_{11}H_{24}O$	76.67	14.04	76.55	13.19	14.0	14.3[a]	—
Tridecyl	$C_{13}H_{28}O$	77.93	14.09	77.80	13.93	30.5	30.5[b]	27.7
Pentadecyl	$C_{15}H_{32}O$	78.87	14.12	79.11	14.17	45.0	45.0[c]	38.0
Heptadecyl	$C_{17}H_{36}O$	79.61	14.15	79.47	14.23	54.0	54.0[d]	46.0
Nonadecyl	$C_{19}H_{40}O$	80.20	14.17	80.38	14.12	62.5	63.0[e]	51.0
Heneicosyl	$C_{21}H_{44}O$	80.69	14.19	80.53	14.10	69.0	69.0[e]	55.0
Tricosyl	$C_{23}H_{48}O$	81.10	14.20	81.30	14.14	72.5	73.1[f]	63.0
Pentacosyl	$C_{25}H_{52}O$	81.44	14.21	81.45	14.16	77.5	77.3[f]	68.0

* Melting points are uncorrected.

** When a sample is cooled below its freezing point, transition appears with change of the transparent waxy material into an opaque crystalline state.

a) R. Robinson, *J. Chem. Soc.*, **125**, 229 (1924).

b) J. Blau, *Monatshe. Chem.*, **26**, 106 (1905).

c) E. Jeffreys, *Am. Chem. J.*, **22**, 28 (1899).

d) P. A. Leven et al., *J. Boil. Chem.*, **20**, 531 (1915).

e) P. A. Leven et al., ibid., **59**, 915 (1924).

f) S. Shiina, *J. Soc. Chem. Ind., Japan* (*Kōgyō Kwagaku Zassi*), **39**, 345 (1936).

TABLE II. FATTY ACIDS

Acids	m. p., °C	Acid value Expt.	Acid value Calcd.	Iodine value	Methyl esters m. p., °C	Methyl esters b. p., °C
Lauric	43.0	279.0	280.2	0	—	110/4 mm.
Myristic	53.5	244.2	245.8	0	18.0	140/4 mm.
Palmitic	62.3	218.6	219.0	0.02	29.0	160/5 mm.
Stearic	69.6	196.5	197.4	0	38.5	178/4 mm.
Behenic	79.5	164.0	164.9	0.1	48.0*	185/1.8 mm.

* Ethyl ester.

diazononadecanone which had been synthesized by Grundmann previously$^{4)}$. The conversion of the diazoketone into methyl nonadecanoate with silver oxide in methanol was carried out easily. The ester was reduced with lithium aluminum hydride to nonadecanol in almost quantitative yield.

Method C which was used for the synthesis of tricosanol $C_{23}H_{47}OH$ and pentacosanol $C_{25}H_{51}OH$ is analogous to that of Bowman's ketone synthesis$^{5)}$. Ethyl *n*-hexane-1, 1, 6-tricarboxylate (II) which served as the starting material was prepared from ethyl malonate and ethyl bromocaproate which was obtained from cyclohexanone by the method of Brown$^{6)}$. Benzyl *n*-hexane-1, 1, 6-tricarboxylate derived from the ethyl ester by transesterification with benzyl alcohol was condensed with palmitoyl chloride or stearoyl chloride, to give, after hydrogenation and decarboxylation, 8-ketotricosanoic acid or 8-ketopentacosanoic acid. Reduction to the corresponding fatty acid by Huang-Minlon's method$^{7)}$ was efficient. Ethyl tricosanoate and ethyl pentacosanoate were readily reduced to the desired alcohols with lithium aluminum hydride.

The physical constants and analytical data of the alcohols are given in Table I together with those reported by other workers who had previously synthesized them by different methods. The transition points of C_{19}, C_{21}, C_{23}, C_{25} alcohols were unknown.

Since it is known that sometimes minor impurities, especially homologues, have a marked influence on the transition behavior of long chain compounds, it was felt necessary to obtain the starting fatty acids in high purity. Commercial fatty acids such as lauric, myristic, palmitic, stearic,

---

4) C. Grundmann, *Ann.*, **524**, 37 (1936).

5) R. E. Bowman, *J. Chem. Soc.*, **1950**, 174.

6) G. B. Brown and C. W. H. Partridge, *J. Am. Chem. Soc.*, **66**, 839 (1944).

7) Huang-Minlon, ibid., **68**, 2487 (1946).

and behenic acids were obtained in a pure state by fractionation of the methyl ester through four feet Fenske column followed by saponification and recrystallization. Physical constants and analytical data of these fatty acids are given in Table II.

Experimental

Undecanol, Tridecanol, Pentadecanol, Heptadecanol and Heneicosanol.—These alcohols were prepared from the corresponding fatty acids by method A involving Hunsdiecker's reaction[3]. A typical example is given for the preparation of heneicosanol.

Silver behenate: $C_{21}H_{43}CO_2Ag$—A solution of 20 g. of potassium behenate in 200 ml. of ethanol was stirred on a steam bath while a solution of 13 g. of silver nitrate in 50% aqueous ethanol was added dropwise. The resulting bulky white precipitate was collected on a filter, thoroughly washed four times by suspension in 500 ml. of hot water, air-dried, and brought to complete dryness at 150°C under reduced pressure (2 mm.). The yield was almost quantitative.

Heneicosyl bromide: $C_{21}H_{43}Br$—The reaction was carried out under strict exclusion of moisture. To a suspension of 12 g. of silver behenate in 80 ml. of carbon tetrachloride was added a solution of 10 g. of bromine in 50 ml. of carbon tetrachloride which had previously been dried over phosphorus pentoxide. Reaction began immediately, with the evolution of carbon dioxide. When the reaction almost ceased, the reaction mixture was heated at the boiling point for a short period to complete the reaction. Silver bromide formed was filtered off and the solution was washed successively with water, sodium thiosulfate solution, 5% sodium hydroxide solution, and water, and dried over sodium sulfate. Evaporation of the solution gave 8.5 g. of an oily product, which solidified on standing at room temperature. Recrystallization from ethanol yielded the pure bromide which melted at 44.5~45°C and weighed 5.3 g. (53%).

Anal. Found: C, 67.5; H, 11.49. Calcd. for $C_{21}H_{43}Br$: C, 67.2; H, 11.47%.

The melting point is higher than that of docosyl bromide $C_{22}H_{45}Br$ (44°C)[8]. This is consistent with the fact that the melting points of normal alkyl bromides of odd carbon numbers are slightly higher than those of next higher homologue.

Heneicosanol: $C_{21}H_{43}CH$ — An intimate mixture of 5 g. of heneicosyl bromide and 2.3 g. of silver acetate was kept at 150°C for 3 hr. The reaction mixture was extracted three times with hot benzene. The benzene solution free from silver bromide was washed with water and dried over sodium sulfate. Evaporation of the solution gave 4.2 g. of a residue which was saponified without purification. The crude ester was refluxed for 3 hr. with 10 ml. of 30% alcoholic potassium hydroxide. The resulting alcohol was recrystallized twice from ethanol and twice from benzene to give heneicosanol in platelets, m. p. 68.5~69°C. Overall yield was 40% (3 g.).

Nonadecanol. — The intermediate diazoketone was prepared by the method of Grundmann[4]. The melting point of this compound was 69~70°C (reported 69°C).

Methyl nonadecanoate: $C_{18}H_{37}CO_2CH_3$—A slurry of freshly prepared silver oxide in methanol was added portionwise to a stirred solution of 18 g. of 1-diazo-2-nonadecanone in 160 ml. of methanol which was heated beforehand at 65°C. The addition required about 4 hr. and the temperature of the reaction mixture was kept at 60~65°C during the course of the reaction. At the end of this period a 2 ml. portion was taken from the solution and added to concentrated hydrochloric acid. An evolution of nitrogen was not observed, and then the solution was cooled and filtered. Partial removal of the methanol and subsequent cooling gave a white solid which was recrystallized from methanol, m. p. 42~43°C. The yield was 17 g. (95%). It was identified by the mixed melting point with an authentic sample.

Reduction of methyl nonadecanoate.—To a stirred suspension of 0.2 g. of lithium aluminum hydride in 25 ml. of dry ether was added a solution of 3 g. of methyl nonadecanoate in 15 ml. of ether dropwise at such a rate that a gentle reflux of the solvent was maintained. After the addition was complete, the solution was refluxed for 15 min. The excess of lithium aluminum hydride was decomposed by cautious addition of water and the reaction mixture was acidified with dilute sulfuric acid. The ether layer was removed, and washed with water to neutral reaction. The solid residue, obtained by removal of the solvent from the dried solution, was recrystallized four times from benzene to give nonadecanol in platelets, m. p. 62~62.5°C. Yield was 90% (2.3 g.).

Tricosanol. — The preparation of intermediate ethyl ε-bromocaproate (I) was modelled after that of Brown and Partridge[6]. From 50 g. of purified cyclohexanone 52 g. of the bromoester was obtained, b. p. 118°C/14 mm. or 98°C/4.5 mm., n_D^{32} 1.4561 (reported: b. p. 120~125°C/14 mm., n_D^{21} 1.4566).

Ethyl n-hexane 1, 1, 6-tricarboxylate (II).—The bromoester (33 g.) was refluxed with a solution of 48 g. of sodiomalonic ester in 150 ml. of absolute ethanol for 8 hr. After removal of the solvent the cooled mixture was treated with dilute solfuric acid and the triethylester was isolated in a usual manner as a colorless liquid, b. p. 150~151°C/1 mm. Yield, 28 g. (63%). n_D^{28}, 1.4360.

Anal. Found: C, 59.91; H, 9.01; Calcd. for $C_{15}H_{26}O_6$: C, 59.58; H, 8.67%.

8-Ketotricosanoic acid (V): $CH_3(CH_2)_{14}CO(CH_2)_6$-$CO_2H$—In a 200 ml. three-necked flask equipped with a mechanical stirrer, a dropping funnel and a reflux condenser fitted with a calcium chloride tube, were placed 0.75 g. of finely powdered sodium sand and 70 ml. of dry benzene. To the mixture was added from the dropping funnel 11.3 g. of ethyl *n*-hexane-1, 1, 6-tricarboxylate.

---

8) V. Braun et at., *Ann.*, 472, 132 (1929).

The mixture was refluxed with stirring until the sodium sand disappeared. It required about 8 hr. After 7.5 g. of benzyl alcohol (purified by oximation followed by distillation: b. p. 79~80°C/7 mm., odorless) was added, the reflux condenser was replaced by a Fenske column and the mixture was heated to distill off ethanol as the benzene-ethanol azeotrope. Then the Fenske column was again replaced by the reflux condenser. Palmitoyl chloride (9 g.) b. p. 148°C/1.5 mm. was added with stirring, and the resulting solution was refluxed for 1 hr. The neutral solution obtained was distilled under reduced pressure to give a yellow oil which could not be crystallized and was subjected to hydrogenation without purification. A solution of 25 g. of tribenzyl compound IV in 50 ml. of ethyl acetate was shaken with Pd-C (0.5 g.) and Pd-$SrCO_3$ (0.5 g.) in a hydrogen atmosphere of slightly positive pressure. After 10 hr. the absorption of hydrogen ceased, but during this period the fresh catalyst was added from time to time because of its poisoning, the total amount of catalyst being 4 g. The solution freed from the catalyst was refluxed for 30 min. to decarboxylate the product. After the solvent was partially removed, white small crystals separated out from the cooled solution. Repeated recrystallization from acetone gave white crystals having the constant melting point of 93.5~94°C. Yield was 23% (2.8 g.).

Anal. Found: C, 75.16; H, 12.00. Calcd. for $C_{23}H_{44}O_3$: C, 74.94; H, 12.03%.

Tricosanoic acid (VI): $C_{22}H_{45}CO_2H$—To a solution of 2.5 g. of potassium hydroxide in 30 ml. of diethylene glycol was added 2.5 g. of the ketonic acid and 2.5 ml. of hydrazine hydrate. The mixture was heated to 165°C in an oil bath. After 1 hr. of heating the water formed distilled off through a take-off condenser. The contents of the flask were held at 200°C for 6 hr., and cooled. The fatty acid was isolated by pouring the reaction mixture into an equal volume of water followed by acidification with dilute sulfuric acid. Recrystallization from benzene gave 2.2 g. of platelets, m. p. 78.5°C (reported: 79~79.3°C[9]). The ethyl ester of the acid was obtained by the usual method and purified by vacuum distillation followed by recrystallization from benzene, m. p. 51~52°C (reported: 51.2~51.4°C[9]), b. p. 207°C/1.5 mm.

Tricosanol: $C_{23}H_{47}OH$ — From 2 g. of ethyl tricosanoate, 0.15 g. of lithium aluminum hydride in absolute ether was obtained 1.3 g. of the pure alcohol which melted at 72.5°C.

Pentacosanol.—It was prepared analogously to tricosanol stearic acid, being used in place of palmitic acid. The experimental results are given briefly.

Condensation product of benzyl n-hexane-1,1,6-tricarboxylate with stearoyl chloride. — From 17 g. of the tribenzyl compound and 11 g. of stearoyl chloride (b. p. 169°C/1.5 mm.) were obtained 24 g. of a crude product in a state of viscous brown liquid.

8-Ketopentacosanoic acid: $CH_3(CH_2)_{16}CO(CH_2)_6CO_2H$—From 24 g. of the above benzyl compound, 2.5 g. of the ketonic acid was obtained. The product was recrystallized from acetone and then from benzene to a constant melting point of 97°C.

Anal. Found: C, 75.91; H, 12.05. Calcd. for $C_{25}H_{48}O_3$: C, 75.70; H, 12.20%.

Pentacosanoic acid: $C_{24}H_{49}CO_2H$ — The Huang-Minlon reduction of 2.5 g. of the ketonic acid gave 2.2 g. of pentacosanoic acid, m. p. 83.1°C (reported: 83.2~83.4°C[9]). Ethyl pentacosanoate, m. p. 57~58°C (reported: 57.1~57.4°C[9]), b. p. 215°C/0.7 mm.

Pentacosanol: $C_{25}H_{51}OH$ — By use of lithium aluminum hydride (0.15 g.), 1.7 g. of the pure product was obtanied from 2.1 g. the ethyl pentacosanoate. m.p. 77.5°C (from ligroin).

The author expresses his sincere thanks to Professor Ryozo Goto for his kind guidance througout this study. Thanks are also due to the Ministry of Education for a Grant-in-Aid for Scientific Research.

Department of Applied Chemistry
Himeji Technical College
Idei, Himeji

---

[9] S. Shiina, *J. Soc. Chem. Ind., Japan* (*Kôgyô Kwagaku Zassi*), **39**, 345 (1936).